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#### **REMARKS**

Claims 14-31 are pending and under examination in the subject application. Applicants note that on page 1 of the July 5, 2007 Office Action, i.e. the Office Action Summary, the Examiner indicated under the heading, "Disposition of Claims," that claims 14-30 are pending in the subject application and subject to a restriction and/or election requirement. Applicants maintain that claims 14-31 are currently pending in the subject application and that the July 5, 2007 Office Action contains a typographical error on page 1. Applicants filed a Preliminary Amendment together with the subject application as originally filed on February 24, 2004. The February 24, 2004 Preliminary Amendment canceled claims 1-13 without prejudice or disclaimer to applicants' right to pursue the subject matters of those claims in the future, leaving original claims 14-31 pending in the subject application. The claims of the subject application have not been further amended since the February 24, 2004 Preliminary Amendment. Furthermore, the subject application was published on November 18, 2004 as U.S. Patent Application Publication No. 2004/0229886 A1. Page 19 of the published application indicates that claims 1-13 are canceled and claims 14-31 are pending. Accordingly, the July 5, 2007 Office Action should have indicated that claims 14-31, rather than claims 14-30, are pending and subject to a restriction and/or election requirement.

#### **Species Election**

In the July 5, 2007 Office Action, the Examiner required the election of one of the following disease models for evaluating the effectiveness of a candidate inhibitor of spermidine biosynthesis:

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- (i) chondrocyte proliferation;
- (ii) chondrocyte final differentiation;
- (iii) angiogenesis; or
- (iv) osteoclastogenesis.

In response, applicants hereby elect, with traverse, species ii, i.e. chondrocyte final differentiation.

Applicants note that each of claims 14-31 read on the elected species.

Applicants respectfully request that the Examiner reconsider and withdraw the species election requirement set forth in the July 5, 2007 Office Action because claims 14-31 are directed to a single invention, rather than patentably distinct inventions. Specifically, the subject invention comprises a method of identifying an inhibitor of spermidine synthase by testing an inhibitor in model systems amenable to assessing the physiological effects of reducing spermidine synthase.

Applicants note that the specification discloses at page 4 that the inventors set out to identify target genes that code for specific factors that stimulate or inhibit the differentiation of progenitor cells to chondrocytes and/or stimulate or inhibit the differentiation of progenitor cells to osteoblasts. In addition, changes in gene expression caused by IL-1, FGF-2 and mechanical stress may be connected to OA development, and, therefore, should be opposed by therapeutic intervention. Example 2 (pages 44-50) indicates that, for the purpose of discovering genes to be targeted for the development of anti-OA drugs, human mesenchymal stem cell (HMSCs) were exposed to a panel of treatments which caused either chondrogenic (e.g. IGF-1) or osteogenic and angiogenic (e.g. IL-1 $\beta$  and FGF-2) responses. Thus, each of

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species i-iv comprises a model system useful for the single purpose of evaluating the effectiveness of a candidate inhibitor of spermidine synthase. Accordingly, species i-iv are not patentably distinct.

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**SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT**

In accordance applicants' duty of disclosure under 37 C.F.R. §1.56 and §1.97(a)-(d), applicants submit this Supplemental Information Disclosure Statement to supplement the Information Disclosure Statement filed February 24, 2004. Applicants direct the Examiner's attention to the following references which are listed on the Substitute Form PTO-1449 attached hereto as **Exhibit A**:

1. U.S. Patent No. 6,696,454 B2 (Bar et al.), issued February 24, 2004;
2. International Publication No. WO 02/058623 A2 (Quark Biotech, Inc. et al.), published August 1, 2002 (**Exhibit 1**);
3. Claims issued in U.S. Patent No. 6,696,454 B2 (Bar et al.), issued February 24, 2004 (**Exhibit 2**);
4. Office Action issued on February 11, 2003 in connection with U.S. Serial No. 10/023,038, filed December 12, 2001, now U.S. Patent No. 6,696,454 B2, issued February 24, 2004 (**Exhibit 3**);
5. Office Action issued on May 1, 2003 in connection with U.S. Serial No. 10/023,038, filed December 12, 2001, now U.S. Patent No. 6,696,454 B2, issued February 24, 2004 (**Exhibit 4**);
6. Nakashim K, (1986) Synthesis of N-chlorosulfonyl Dicyclohexylamine as a Potent Inhibitor for Spermidine Synthase and Its Effects on Human Leukemia MOLT4B

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*Cells. Biochem. Biophys. Res. Commun.* 141:718-722; and

7. International Preliminary Examination Report issued by the International Preliminary Examining Authority (IPEA/US) on September 3, 2003 in connection with International Application No. PCT/US01/48192 (**Exhibit 5**).

Copies of documents numbers 2-5 and 7 are attached hereto as **Exhibits 1-5**, respectively.

The above-identified application is a continuation of U.S. Serial No. 10/023,038, now U.S. Patent No. 6,696,454 B2 (document number 1), issued February 24, 2004. Applicants maintain that documents number 6 was previously cited by the Examiner in a May 1, 2003 Office Action (document number 5) in connection with U.S. Serial No. 10/023,038.

Under 37 C.F.R. §1.98(d), copies of references which were previously cited by, or submitted to, the U.S. Patent and Trademark Office in an application relied upon for an earlier filing date under 35 U.S.C. §120 are not required to be submitted in the later application. Accordingly, a copy of document number 6 is not submitted herewith.

Furthermore, under 37 C.F.R. §1.98(a)(2)(ii), copies of U.S. Patents and U.S. Patent Application Publications need not be provided. Accordingly, a copy of document number 1 is not submitted herewith.

The Examiner is respectfully requested to make the above-listed references of record in the subject application by initialing and dating the attached Substitute Form PTO-1449, and returning a

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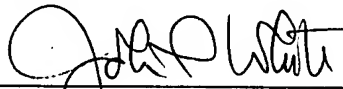
copy of the initialed and dated form to applicants' undersigned attorney.

This Supplemental Information Disclosure Statement is being submitted pursuant to 37 C.F.R. §1.97(c)(2) before the mailing of a Final Office Action. Pursuant to 37 C.F.R. §1.17(p), the fee for filing this Supplemental Information Disclosure Statement is ONE HUNDRED AND EIGHTY DOLLARS (\$180.00) and a check including this amount is enclosed.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorney invites the Examiner to telephone him at the number provided below.

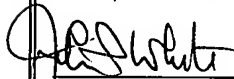
No fee, other than the enclosed fee of \$1,230.00, including \$1,050.00 for a three-month extension of time and \$180.00 for filing the Supplemental Information Disclosure Statement, is deemed necessary in connection with the filing of this Communication. If any additional fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully submitted,



John P. White  
Registration No. 28,678  
Attorney for Applicants  
Cooper & Dunham LLP  
1185 Avenue of the Americas  
New York, New York 10036  
(212) 278-0400

I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450



October 31, 2007  
John P. White Date  
Reg. No. 28,678

**EXHIBIT A**

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